

Claims:

1. A system comprising:
 - a visible light source providing light over a range of wavelengths that includes one or more wavelengths of visible light;
 - 5 an excitation light source providing light at one or more wavelengths outside the range of wavelengths of the visible light source, the one or more wavelengths selected to excite a fluorescent substance, which emits one or more photons at an emission wavelength;
 - an electronic imaging device;
 - 10 an optical guide having a first end with a lens that captures an image of a subject and a second end that couples the image to the electronic imaging device; and
 - a filter for coupling the visible light source and the excitation light source into the optical guide, the filter reflecting some of the light provided by the visible
 - 15 light source and some of the light from the excitation light source toward the subject, the filter further transmitting some visible light from the subject captured by the lens toward the electronic imaging device, and the filter further transmitting the emission wavelength from the subject captured by the lens toward the electronic imaging device.
- 20 2. A system comprising:
 - a visible light source illuminating a subject, the visible light source providing a range of wavelengths including one or more wavelengths of visible light;
 - an excitation light source illuminating the subject, the excitation light source
 - 25 providing an excitation wavelength that is not one of the one or more wavelengths of visible light;
 - a fluorescent substance introduced into a circulatory system of the subject, the fluorescent substance being soluble in blood carried by the circulatory system and the fluorescent substance emitting photons at an emission wavelength in
 - 30 response to the excitation wavelength;
 - an electronic imaging device that captures an image of a field of view that includes some portion of the subject and the circulatory system of the subject, the

image including a first image obtained from the one or more wavelengths of visible light and a second image obtained from the emission wavelength; and

a display that renders the first image and the second image, the second image being displayed at a visible light wavelength.

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3. A system comprising:

an operating area closed to ambient light, the operating area including a surgical field where a surgical procedure may be performed on a subject;

10 a visible light source illuminating the surgical field, the visible light source providing a range of wavelengths including one or more wavelengths of visible light;

an excitation light source illuminating the surgical field, the excitation light source including at least one wavelength outside the range of wavelengths of visible light;

15 a fluorescent substance suitable for in vivo use, the fluorescent substance fluorescing at an emission wavelength in response to the at least one wavelength of the excitation light source, the fluorescent substance being introduced into the surgical field;

20 an electronic imaging device that captures a visible light image of the surgical field and an emission wavelength image of the surgical field; and

a display that renders the visible light image and the emission wavelength image of the surgical field, the emission wavelength image being displayed at a visible light wavelength.

25 4. A system comprising:

a visible light source that illuminates a subject, the visible light source providing a range of wavelengths including one or more wavelengths of visible light;

30 an excitation light source that illuminates the subject at the same time that the visible light source illuminates the subject, the excitation light source providing an excitation wavelength that is not one of the one or more wavelengths of visible light;

a fluorescent substance introduced into a circulatory system of the subject, the fluorescent substance being soluble in blood carried by the circulatory system and the fluorescent substance emitting photons at an emission wavelength in response to the excitation wavelength; and

5 an electronic imaging device that captures an image of a field of view that includes some portion of the subject and the circulatory system of the subject, the image including a first image obtained from the one or more wavelengths of visible light and a second image concurrently obtained from the emission wavelength.

10 5. The system of any of claim 1, 2, 3, or 4 wherein the one or more wavelengths of visible light from the visible light source does not include far-red light, at least one of the excitation light source and the emission wavelength including a far-red light wavelength.

15 6. The system of claim 1 wherein the filter is a dichroic mirror placed in the optical guide at a forty-five degree angle to a central axis of the optical guide.

7. The system of any of claims 1 through 6 further comprising a second filter that separates the emission wavelength from the range of wavelengths from the
20 visible light source, the emission wavelength being directed toward a first optical transducer of the electronic imaging device and the range of wavelengths from the visible light source being directed toward a second optical transducer of the electronic imaging device.

25 8. The system of any of claims 1 through 6 further comprising a second filter that separates the emission wavelength from the range of wavelengths from the visible light source, the emission wavelength being directed toward a first optical transducer of the electronic imaging device and the range of wavelengths from the visible light source being directed toward a second optical transducer of the
30 electronic imaging device wherein the second optical transducer separately senses at least each one of red, green, and blue light intensities.

9. The system of any of claims 1-6 further comprising a second filter that separates the emission wavelength from the range of wavelengths from the visible light source, the emission wavelength being directed toward a first optical transducer of the electronic imaging device and the range of wavelengths from the visible light source being directed toward a second optical transducer of the electronic imaging device wherein the second optical transducer separately senses at least each one of cyan, magenta, and yellow light intensities.
10. The system of any of claims 1-6 further comprising a second filter that separates the emission wavelength from the range of wavelengths from the visible light source, the emission wavelength being directed toward a first optical transducer of the electronic imaging device and the range of wavelengths from the visible light source being directed toward a second optical transducer of the electronic imaging device wherein the second filter includes a dichroic mirror that reflects the emission wavelength and transmits the one or more wavelengths of visible light from the visible light source.
11. The system of any of claims 1-6 further comprising a second filter that separates the emission wavelength from the range of wavelengths from the visible light source, the emission wavelength being directed toward a first optical transducer of the electronic imaging device and the range of wavelengths from the visible light source being directed toward a second optical transducer of the electronic imaging device wherein the second filter includes a dichroic mirror that reflects the one or more wavelengths of visible light from the visible light source and transmits the emission wavelength.
12. The system of any of claims 1-6 further comprising a second filter that shapes the wavelengths of the visible light source.
13. The system of any of claims 1 through 12 wherein the electronic imaging device includes at least one charge-coupled device.

14. The system of any of claims 1 through 12 wherein the electronic imaging device includes a video camera sensitive to visible light.

15. The system of any of claims 1 through 12 wherein the electronic imaging device includes an emission wavelength camera.

16. The system of any of claims 1 through 12 wherein the electronic imaging device captures a visible light image and an emission wavelength image, the system further comprising a processor that converts the emission wavelength image to a converted image having one or more visible light components, and combines the converted image with the visible light image for display.

17. The system of any of claims 1 through 12 wherein the electronic imaging device captures a visible light image and an emission wavelength image, the system further comprising a processor that converts the emission wavelength image to a converted image having one or more visible light components, and superimposes the converted image onto the visible light image for display.

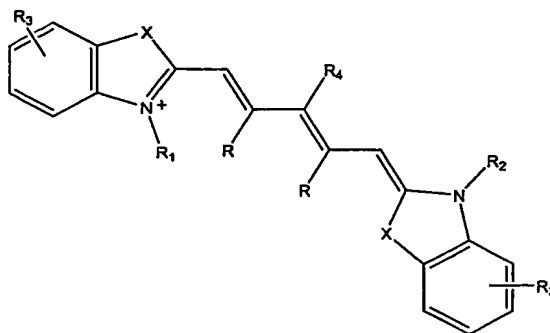
18. The system of any of claims 1 through 12 wherein the electronic imaging device captures a visible light image and an emission wavelength image, and wherein the visible light image is captured at thirty frames per second and the emission wavelength is captured at fifteen frames per second, the emission wavelength being converted to thirty frames per second for combination with the visible light image.

19. The system of any of claims 1 through 12 wherein the electronic imaging device captures a visible light image and an emission wavelength image, and wherein the visible light image is captured at thirty frames per second and the emission wavelength is captured at fifteen frames per second, the visible light image being converted to fifteen frames per second for combination with the emission wavelength image.

20. The system of any of claims 1 through 19 wherein the excitation light source includes a laser.
21. The system of any of claims 1 through 19 further comprising a display that displays images captured by the electronic imaging device.
22. The system of any of claims 1 through 21 wherein the fluorescent substance labels at least one of an antibody, an antibody fragment, or a low-molecular-weight ligand that accumulates at a lesion, the system being used to visualize the lesion.
23. The system of any of claims 1 through 21 wherein the fluorescent substance is soluble in blood, the system being used to visualize a blood system.
24. The system of claim 2 wherein the display renders the second image of the circulatory system superimposed on the first image of the subject.
25. The system of any of claims 1 through 24 wherein the fluorescent substance is a fluorescent dye injected into the subject by an intravenous injection.
26. The system of any of claims 1 through 24 wherein the fluorescent substance sprayed onto the subject.
27. The system of any of claims 1 through 21 wherein the fluorescent substance is one or more quantum dots.
28. The system of any of claims 2, 3, or 5-21 wherein the display is provided to a physician for use during a procedure, the procedure being at least one of a diagnostic procedure or a therapeutic procedure.
29. The system of any of claims 2, 3 or 5-21 wherein the display includes a surgical microscope.

30. The system of any of claims 1-26 wherein the fluorescent substance includes at least one of indocyanine green; fluorescein; methylene blue, and IRDye78-CA.

31. The system of any of claims 1-21 wherein the fluorescent substance is a dye
5 having a structure of the formula:



wherein, as valence and stability permit,

X represents C(R)₂, S, Se, O, or NR₅;

R represents H or lower alkyl, or two occurrences of R, taken together, form a ring
10 together with the carbon atoms through which they are connected;

R₁ and R₂ represent, independently, substituted or unsubstituted lower alkyl, lower alkenyl, cycloalkyl, cycloalkylalkyl, aryl, or aralkyl;

R₃ represents, independently for each occurrence, one or more substituents to the ring to which it is attached;

15 R₄ represents H, halogen, or a substituted or unsubstituted ether or thioether of phenol or thiophenol; and

R₅ represents, independently for each occurrence, substituted or unsubstituted lower alkyl, cycloalkyl, cycloalkylalkyl, aryl, or aralkyl.

20 32. A system comprising:

a visible light means for illuminating a subject with one or more wavelengths of visible light;

an excitation light means for illuminating the subject with an excitation wavelength that is not one of the one or more wavelengths of visible light;

a fluorescence means introduced into a subject, the fluorescence means for dissolving in blood carried by the circulatory system and for emitting photons at an emission wavelength in response to the excitation wavelength;

an imaging means for capturing a visible light image of the subject and an
5 emission wavelength image of the circulatory system of the subject; and

a display means for concurrently rendering the visible light image of the subject and the emission wavelength image of the circulatory system.

33. A method comprising:

10 illuminating a subject with one or more wavelengths of visible light;
concurrently illuminating the subject with an excitation wavelength that is not one of the one or more wavelengths of visible light;

introducing a fluorescent substance into a circulatory system of the subject, the fluorescent substance being soluble in blood carried by the circulatory system
15 and the fluorescent substance emitting photons at an emission wavelength in response to the excitation wavelength;

electronically capturing a visible light image of the subject;

electronically capturing an emission wavelength image of the subject that shows the circulatory system; and

20 displaying concurrently the visible light image of the subject and the emission wavelength image of the circulatory system.

34. A method comprising:

enclosing a subject in an operating area closed to ambient light;

25 illuminating the subject with one or more wavelengths of visible light;
concurrently illuminating the subject with an excitation wavelength that is not one of the one or more wavelengths of visible light;

introducing a fluorescent substance into the subject, the fluorescent substance emitting photons at an emission wavelength in response to the excitation
30 wavelength;

electronically capturing a visible light image of the subject;

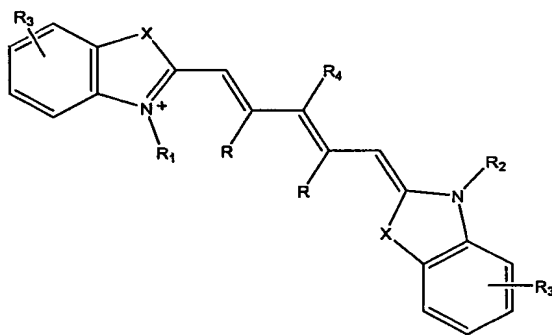
electronically capturing an emission wavelength image of the subject; and

displaying concurrently the visible light image and the emission wavelength.

35. A method comprising:
providing one or more wavelengths of visible light;
5 providing an excitation wavelength that is not one of the one or more wavelengths of visible light;
introducing a fluorescent substance into a subject, the fluorescent substance emitting photons at an emission wavelength in response to the excitation wavelength;
10 providing a laparoscope having a first optical path that directs the one or more wavelengths of visible light toward a subject, a second optical path that directs the excitation wavelength toward the subject, and a third optical path that directs an emission wavelength and the one or more wavelengths of visible light from the subject to an imaging device;
15 making an incision in a body that includes the subject;
directing the laparoscope into the incision so that the subject is within a field of view of the laparoscope; and
displaying concurrently a visible light image of the subject and the emission wavelength image of the subject.
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36. The method of claim 35 wherein at least two of the first optical path, the second optical path, and the third optical path are coaxial.
37. A method comprising:
25 providing one or more wavelengths of visible light;
providing an excitation wavelength that is not one of the one or more wavelengths of visible light;
introducing a fluorescent substance into a subject, the fluorescent substance emitting photons at an emission wavelength in response to the excitation
30 wavelength;
providing an endoscope having an optical path for directing images of the subject to an imaging device;

coupling the excitation wavelength and the one or more wavelengths of visible light into the optical path;
 directing the endoscope into a body so that the subject is within a field of view of the endoscope;
 5 capturing an emission wavelength image of the subject and a visible light image of the subject at the imaging device; and
 displaying concurrently the visible light image of the subject and the emission wavelength image of the subject.

- 10 38. The method of any of claims 33-37 wherein the fluorescent substance is a dye having a structure of the formula:



wherein, as valence and stability permit,

X represents C(R)₂, S, Se, O, or NR₅;

- 15 R represents H or lower alkyl, or two occurrences of R, taken together, form a ring together with the carbon atoms through which they are connected;

R₁ and R₂ represent, independently, substituted or unsubstituted lower alkyl, lower alkenyl, cycloalkyl, cycloalkylalkyl, aryl, or aralkyl;

- R₃ represents, independently for each occurrence, one or more substituents to the ring to which it is attached;

20 R₄ represents H, halogen, or a substituted or unsubstituted ether or thioether of phenol or thiophenol; and

R₅ represents, independently for each occurrence, substituted or unsubstituted lower alkyl, cycloalkyl, cycloalkylalkyl, aryl, or aralkyl.